PATENT
Docket No. 252312005704

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Jennifer Bushard

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Stephen M. COUTTS et al.

Serial No.: To be assigned
Continuation of U.S.S.N. 08/769,041

Filing Date: Filed Herewith

For: CONJUGATES OF CHEMICALLY DEFINED NON-POLYMERIC VALENCY PLATFORM MOLECULES AND BIOLOGICALLY ACTIVE MOLECULES (AS AMENDED)

Examiner: To be assigned

Group Art Unit: To be assigned

PRELIMINARY AMENDMENT

Box PATENT APPLICATION
Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Prior to examination of this application on the merits, please enter the amendments below.

AMENDMENTS

In the Title:

Please delete the Title and replace it with --Conjugates of Chemically Defined Non-Polymeric Valency Platform Molecules and Biologically Active Molecules--.

In the Cross Reference to Related Applications:

Please delete the entire paragraph on page 1 under the heading "Cross Reference to Related Applications," and substitute therefore the following paragraph:

--This application is a continuation of U.S. Patent Application Serial No. 08/769,041, filed December 18, 1996, which is a divisional of U.S. Patent Application Serial No. 08/453,254, filed May 30, 1995, now U.S. Patent No. 5,606,047, which is a continuation of U.S. Patent Application Serial No. 08/152,506, filed November 15, 1993, now U.S. Patent No. 5,552,391, which is a continuation-in-part of U.S. Patent Application Serial No. 07/914,869 filed July 15, 1992, now U.S. Patent No. 5,276,013; and a continuation-in-part of U.S. Patent Application Serial No. 08/118,055, filed September 8, 1993, now U.S. Patent No. 6,060,056. The disclosures of each of these parent applications and patents are incorporated herein by reference.--

In the Specification:

On page 2, line 31, delete "Saski" and insert --Sasaki--;

line 33, delete "(987)" and insert --(1987)--.

On page 3, line 14, delete "fluctuates" and insert --fluctuate--;

line 24, delete "chemical" and insert --synthetic--;

line 29, delete "chemical" and insert --synthetic--.

On page 4, line 30, delete "polyglycol" and insert --polyether--.

On page 5, line 1, delete "$C(CH_2OCH_2CH_2\text{-})_s(OH)_{4-s}$" and insert --$C(CH_2OCH_2CH_2\text{-})_s(CH_2\ OH)_{4-s}$--;

line 18, delete "$S(=O)CR^B{=}CR^B{}_2$" and replace it with

--$S(=O)_2CR^B=CR^B{}_2$--;

line 24, delete "-C(=O)CHCHC(=O)-" and insert

---C(=O)CH=CHC(=O)-;

line 25, delete "$S(=O)CR^B=CR^B{}_2$" and replace it with

--$S(=O)_2CR^B=CR^B{}_2$--.

On page 10, line 15, delete "chemical" and insert --synthetic--.

On page 12, line 20, delete "$C(CH_2OCH_2CH_2-)_s(OH)_{4-s}$" and insert

--$C(CH_2OCH_2CH_2-)_s(CH_2\ OH)_{4-s}$ --.

On page 13, lines 1 and 10, delete "-C(=O)CHCHC(=O)-" and insert

---C(=O)CH=CHC(=O)-.

On page 15, line 15, after "shown," insert --or with saline--.

On page 17, line 33, after "itself" insert --or when administered as the platform portion of a conjugate--.

On page 19, line 11, after "antibody" insert --and or apoptosis--.

On page 20, line 13, delete "chemical" and insert --synthetic--;

line 17, delete "chemical" and insert --synthetic--.

On page 25, line 10, delete "phosphormidate" and insert --phosphoramidite--.

On page 26, line 12, delete "α-sperm" and insert --sperm--.

On page 27, line 6, delete "eptiopes" and insert --epitopes--.

On page 29, lines 8 and 9, delete "is reacted in the presence of $NaCNBH_3$ with animo platforms to form conjugates" and insert --are reacted with amino platforms in the presence of $NaCNBH_3$ to form conjugates--.

line 11, delete "glycol-lipids" and insert --glycolipids--.

On page 30, line 23, delete "dimethyl formamide" and insert --dimethylformamide--;

line 28, delete "N-methylmorpholine oxide" and insert

--N-methylmorpholine-N-oxide--.

On page 86, line 9, delete "Hydroxysuccinimidyl" and insert --Succinimidyl";

On page 95, line 18, delete "μM" and insert --μmol--.

line 19, delete "μM" and insert --μmol--.

On page 99, line 3, after "synthesis" insert --which incorporates the elements of an acyclic triol moiety (ACT)";

line 7, delete "d-[DMTr-(bzCp(CE)bzA)$_{25}$]" and insert --d-[DMTr-(BzCp(CE)BzA)$_{25}$]--.

On page 100, line 24, after "polynucleotide" insert --,PN-KLH--.

On page 103, line18, before "5' " insert --Tr- --;

line 23, before "5' " insert --Tr- --.

On page 104, line 30, after "nm" insert --,assumed--".

On page 105, line 20, before "5' " insert --Tr- --;

line 23, before "5' " insert --Tr- --.

On page 106, line 23, before "5' " insert --Tr- --;

line 26, before "5' " insert --Tr- --.

On page 119, Table 6, please delete the last entry "8" in the column entitled "Peptide Conjugated" and replace with --9--.

In the claims:

Please cancel claims 2-21 without prejudice or disclaimer.

Please add new claims 22- 45 as follows.

--22. (New) A composition comprising a plurality of a conjugate, wherein said conjugate comprises:

a chemically defined valency platform molecule comprising branching groups, wherein the valency platform molecule contains a specific number of attachment sites whereby the valency of said platform molecule is defined; and

a multiplicity of biologically active molecules conjugated to the chemically defined valency platform molecule at said attachment sites;

wherein the molecular weight of the valency platform molecules is substantially homogeneous; and

wherein the valency platform molecules have attachment sites at the same location.

23. (New) The composition of claim 22, wherein the branching groups are derived from a functional group selected from the group consisting of diamino acid, triamine, and amino diacid.

24. (New) The composition of claim 22, wherein the multiplicity of biologically active molecules are the same.

25. (New) The composition of claim 22 comprising conjugates, wherein a said conjugate comprises four biologically active molecules.

26. (New) The composition of claim 22, wherein the biologically active molecule comprises a polynucleotide.

27. (New) The composition of claim 26, wherein the polynucleotide is a polynucleotide duplex.

28. (New) The composition of claim 26, wherein the polynucleotide is a polynucleotide duplex of 20 to 50 bp in length.

29. (New) The composition of claim 26, wherein the polynucleotide is synthetic.

30. (New) The composition of claim 26, wherein the polynucleotide is prepared by molecular cloning.

31. (New) The composition of claim 26, wherein the polynucleotide is a polynucleotide duplex having a B DNA type helical structure.

32. (New) The composition of claim 22, wherein the biologically active molecule is selected from the group consisting of carbohydrates, lipids, lipopolysaccharides, peptides, proteins, glycoproteins, and drugs.

33. (New) The composition of claim 22, wherein the biologically active molecule is selected from the group consisting of analogs of immunogens, haptens, mimotopes, and aptamers.

34. (New) The composition of claim 22, wherein the chemically defined valency platform molecule is substantially nonimmunogenic.

35. (New) The composition of claim 22, wherein the composition comprises a pharmaceutically acceptable carrier.

36. (New) The composition of claim 35, wherein the composition is suitable for treating antibody mediated pathologies.

37. (New) The composition of claim 35, wherein the composition is suitable for injection.

38. (New) The composition of claim 35, wherein the composition is suitable for the treatment of human systemic lupus erythematosus.

39. (New) The composition of claim 22, wherein the conjugate comprises polyethylene glycol.

40. (New) The composition of claim 22, wherein the valency platform molecule comprises polyethylene glycol.

41. (New) The composition of claim 22, wherein the conjugate comprises polyethylene glycol having the formula $-CH_2(CH_2OCH_2)_rCH_2-$, wherein r=0 to 300.

42. (New) The composition of claim 22, wherein the valency platform molecule comprises polyethylene glycol having the formula $-CH_2(CH_2OCH_2)_rCH_2-$, wherein r=0 to 300.

43. (New) The composition of claim 22, wherein the valency platform molecule comprises triethylene glycol.

44. (New) A method of making the composition of claim 22, the method comprising forming said conjugates by covalently bonding the biologically active molecules to the chemically-defined valency platform molecule to form a conjugate.

45. (New) A method of making the composition of claim 22, wherein the biologically active molecule is a polynucleotide duplex, the method comprising forming said conjugates by:

reacting a multiplicity of single-stranded polynucleotides, each of which is at least about 20 nucleotides in length and has a functional group at or proximate one of its termini, with functional groups on the chemically-defined valency platform molecule to form the conjugate; and

annealing complementary single-stranded polynucleotides to the single-stranded polynucleotides conjugated to the chemically-defined valency platform molecule to form pendant chains of double-stranded DNA. --

REMARKS

Claims 2-21 have been cancelled, without prejudice or disclaimer of any previously claimed subject matter. New claims 22- 45 have been added. No new matter has been introduced.

The specification also has been amended to correct inadvertent typographical errors. In the specification on page 5, a typographical error in the structure of the sulfone, $S(=O)_2$, functionality has been corrected. Support for the amendment appears on page 5, line 18 and lines 25-26, which recite an "α,β-unsaturated sulfone". A sulfone group, as is known in the art, includes two oxygen atoms, and comprises the structure $-S(=O)_2-$.

Support for the new claims is found, for example, on page 3, lines 9-35; page 11, lines 1-19; page 17, lines 19-24; page 19, line 14 - page 20, line 15; page 28, lines 17-34; Figures 6A, 6B, 7, and 13; reaction schemes 1-13; and in the originally filed claims.

Applicants request examination of the claims as amended on the merits.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952 referencing docket number 252312005704**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: December 29, 2000

Respectfully submitted,

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